Appl. No.: 10/620,787

Art Unit: 1648

Reply to Final Office Action of 11/20/06

Patent 51300-00006

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

- 1. (ORIGINAL) A polyprotein comprising external-immunogens of membraneassociated proteins of variola major or immunologically cross-reactive poxviruses.
- 2. (ORIGINAL) An immunogenic composition comprising the polyprotein of claim 1.
 - 3. (WITHDRAWN) An isolated nucleic acid encoding the polyprotein of claim 1.
- 4. (WITHDRAWN) An immunogenic composition comprising the nucleic acid of claim 3.
 - 5. (WITHDRAWN) A eukaryotic cell comprising the nucleic acid of claim 3.
- 6. (WITHDRAWN) The eukaryotic cell of claim 5, wherein the eukaryotic cell is a mammalian cell.
- 7. (ORIGINAL) The polyprotein of claim 1 wherein the immunologically cross-reactive poxvirus is vaccinia virus.
- 8. (ORIGINAL) A polyprotein comprising external immunogens of at least two poxvirus membrane-associated proteins selected from the group consisting of: M1R, A36r, I5R, B7R, F8L, A30L, L1R, A33R, H5R, B5R, D8L and A27L.
- 9. (ORIGINAL) The polyprotein of claim 8 comprising external immunogens of M1R, A30L, and A36R.
- 10. (ORIGINAL) A polyprotein comprising external immunogens of at least two membrane-associated proteins, wherein antibodies against one of the proteins are synergistic with antibodies against the at least one other protein.
- 11. (ORIGINAL) The polyprotein of claim 10 wherein the synergistic antibodies recognize A36R of variola major or A33R of vaccinia.

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12. (WITHDRAWN) A method of inducing an antibody response comprising: administering the polyprotein of claim 1 or 8 to a mammal.

- 13. (WITHDRAWN) A method of inducing an antibody response comprising: administering the immunogenic composition of claim 2 or 4 to a mammal.
- 14. (WITHDRAWN) A method of making an immunogen comprising: identifying a vaccinia protein that induces neutralizing or synergistic antibodies; aligning the protein sequence of the vaccinia protein with its variola homolog; synthesizing a nucleic acid sequence encoding at least an external segment of the variola protein; and causing said nucleic acid to be expressed as a polypeptide.
- 15. (WITHDRAWN) The method of claim 14 wherein the causing step comprises transformation of a eukaryotic cell in vitro.
- 16. (WITHDRAWN) The method of claim 14 wherein the causing step comprises administration of the nucleic acid to a mammal.
- 17. (WITHDRAWN) A method of making an immunogen comprising: identifying a vaccinia protein that induces neutralizing or synergistic antibodies; aligning the protein sequences of multiple isolates of the vaccinia protein with multiple isolates its variola homolog; determing a variola consensus sequence; synthesizing a nucleic acid sequence encoding at least an external segment of said consensus sequence; and causing said nucleic acid to be expressed as a polypeptide.
 - 18. (CANCELED)
 - 19. (CANCELED)
- 20. (ORIGINAL) An immunogenic composition comprising a complex of polypeptides wherein each polypeptide comprises an external immunogen of a membrane-associated protein of variola major or immunologically cross-reactive poxviruses and wherein said complex is not an entire virus.
- 21. (PREVIOUSLY PRESENTED) The immunogenic composition of claim 20 wherein the polypeptides are biotinylated and the complex is formed by the addition of avidin or streptavidin.

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22. (PREVIOUSLY PRESENTED) The immunogenic composition of claim 20 wherein the complex is formed by anchoring the polypeptides in a liposome or micelle.

- 23. (ORIGINAL) A polyprotein comprising external immunogens of membraneassociated proteins of variola major or immunologically cross-reactive poxviruses wherein the individual proteins are joined through a linker-spacer peptide.
- 24. (PREVIOUSLY PRESENTED) The polyprotein of claim 23 wherein the linker-spacer peptide comprises SEQ ID NO. 33.
 - 25. (ORIGINAL) The polyprotein of claim 23 further comprising an affinity tag.
- 26. (ORIGINAL) The polyprotein of claim 25 wherein the affinity tag is a polyhistidine tag.
- 27. (PREVIOUSLY PRESENTED) An immunogenic composition comprising an immunogen made by the method comprising: identifying a vaccinia protein that induces neutralizing or synergistic antibodies; aligning the protein sequences of multiple isolates of the vaccinia protein with multiple isolates of its variola homolog; determining a variola consensus sequence; synthesizing a nucleic acid sequence encoding at least an external segment of said consensus sequence; and causing said nucleic acid to be expressed as a polypeptide.
- 28. (PREVIOUSLY PRESENTED) An immunogenic composition comprising a cocktail of immunogens made by the method comprising: identifying a vaccinia protein that induces neutralizing or synergistic antibodies; aligning the protein sequences of multiple isolates of the vaccinia protein with multiple isolates of its variola homolog; determining a variola consensus sequence; synthesizing a nucleic acid sequence encoding at least an external segment of said consensus sequence; and causing said nucleic acid to be expressed as a polypeptide.
- 29. (NEW) A polyprotein comprising immunogens of one or more membrane associated proteins of variola major or immunologically cross-reactive poxviruses, wherein at least one of said immunogens comprises a polypeptide or protein selected from the group consisting of external immunogens and complete proteins.